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**Sir Anthony Epstein, CBE FRS**  
**in conversation with Dr Denis Burkitt, CMG FRS**  
**Oxford 20 March 1991**

DB I'd like to take this opportunity, Tony, of thanking you once again for the profound influence you've had on my life. Because looking back, I realise how often one's work might be totally sterile unless it is taken up by somebody else with a different perspective, a different background, and as it were made to come to life. Now, I look back with clear memories of the first time that you and I met when I was lecturing to medical students and a few others whom I didn't expect to be interested. I was an unknown chap talking about an unknown something or other, a tumour. You somehow or other - I don't know perhaps you might tell us - came along and sat near the back of my lecture. But that lecture and that meeting was the starting point of tremendous importance; one doesn't recognise it at the time but in actual fact it was one of the most important events of my scientific life. And I might well not have been lecturing at Middlesex; you might well have not have decided to come along. Now, what made you come along to listen to an unknown chap from Africa chatting on what seemed to be a pretty unimportant subject?

AE Well, as I remember it you had actually been before, because you had a connection with David Patey(?) who was the surgeon in charge of the surgical division at the Middlesex Hospital. And in the past you'd come, I think, if I recall rightly, and presented all those bizarre cases, which weren't seen in Western Europe, which were very common and everyday occurrences in your practice in East Africa. But this time you came with a different title and you came and talked about a new tumour, the commonest tumour of children in Africa. And I think it was that that probably caught my eye and as you say I came and sat at the back of you lecture.

DB Now, you see you must have been one of the very scientists at that time who felt a sort of gut feeling that since many tumours in animals were known to be caused by viruses - and [tumours in] birds - you felt it would be strange if humans were somehow different. Now, the scientific establishment as a whole had rather pulled away from the idea that viruses could play a role in human cancer, but you felt intuitively that they could, and that it was probably what gave your persistence to get your teeth into it and hang on to it in spite of, I'm sure, much apparent opposition until you actually found some viruses. Now isn't that about true?

AE Well, I'm glad you actually added the word birds because clearly the first instance of a cancer causing virus in vertebrates was in birds, and that was the Rous sarcoma which was discovered to be caused by a virus in 1911. And of course that was not believed; indeed Peyton Rous didn't get the Nobel Prize until he was eighty-six years old, which was over fifty years after he made his discovery, which underlies I think what you're saying about how people didn't believe that. And the point about the birds is that I was one of the few people in the world still working on the Rous

sarcoma virus. There must have been a handful of people world wide doing that, and we were all considered to be crazy. I mean it was an absurd thing to be doing. But of course when you gave your talk and it became clear that the distribution of this weird tumour, because it was weird - the distribution geographically, as well as in the body; it's weird in the body and geographically. Then you went on and told us about temperature and rainfall dependence. Well, as soon as we got to that, twenty minutes into your talk, I could hardly sit still because it was immediately clear that anything which had its distribution determined by temperature and rainfall had a biological cause. And of course for me working with the Rous sarcoma virus, a tumour virus of animals, it had to be that it was a virus induced tumour in humans, and that so far as I was concerned was it.

DB Well, of course you were, or had a prepared mind. A vast majority of people hearing a talk like that, it wouldn't have spoken to them. But you knew what you were looking for, and then of course this meeting at the Middlesex was the starting point of many years, most of a lifetime, of co-operation because I remember you came up to me after the lecture and asked me if we could send you biopsy material from our tumours, which we did. I didn't actually do the physical sending, it was mostly done by Dennis Wright, but we sent you material. Now, that you see...what a tremendous lot depended on your idea that we should co-operate in that way, of us seeing the tumours in Africa, and you looking at them in England. Because so often research depends on two people doing different things in different places but as it were linking up. Now, that was a great insight on your part and I hope we'll get on in a moment to the fun we had together in Africa looking for monkeys and one thing and another.

AE Before that, you make it sound very easy but, if you remember, you actually came to tea with us two days later and we arranged this dispatch of material. But that was not it, because there was an awful lot of trouble after that, and there was a great deal of scientific politics involved, and much above your level and my level, which held it up for what? - I don't know two or three months. And it wasn't until actually I was enabled to come to visit you in Kampala through the generosity of the British Empire Cancer Campaign, as it then was, now of course the Cancer Research Campaign, who funded the trip. It wasn't until that happened that we actually got the thing to work. So even that was fraught with difficulties of a curious kind which led to a lot of trouble. I never actually got to the bottom of that. The story is known but is kept under wraps because I think both the organisations involved have had histories prepared and this information is known but is being quietly kept under wraps. I don't know whether they have a fifty-year rule or something but you and I won't live to see what's in the box.

DB If I remember rightly, during this political disagreement, time went by and then the Americans got on to it and decided to send a group out to Nairobi. And then both of the British institutions felt it would be a great pity if the Americans got in first and suddenly then things began to happen.

AE That's right, things began to move.

DB Now, how long I wonder after that was it, that you made your first of many trips to our benefit and joy, out in Uganda? You came out to see us.

AE I'm guessing. I think it must have been in September after...your talk was in March.

DB Was it in March?

AE Yes. I think it was the 22<sup>nd</sup> March and I think it was September that I came out. I mean I can easily check it.

DB Now, was it on your first trip or on a subsequent trip that you had the idea that if we could collect monkeys and inject them with tumour material? Was that the idea or was it looking for viruses in the monkeys?

AE No, no. That was much later. That was several years later. Yes that was later. That was when we did experiments to try and pass the tumour to monkeys through the agency of the virus, which by that time we discovered and knew to be there. Of course, we were making a silly mistake, but it's easy to know that with hindsight, because you can't pass EB [Epstein-Barr] virus to old world monkeys because they are all carrying the first cousin of EB virus; they are the monkey EB viruses and so they are partly immune. But you can of course, as we all know now, pass it to South American monkeys.

DB I know, but you did this?

AE Yes, that's been done. Yes of course, and that is of course the standard experimental animal, but nobody knew that at the time.

DB But didn't you even get tumours to grow in...?

AE Well, no I think we probably didn't. I think we probably didn't. We got something, we certainly got something but it's, I mean, not clear-cut like with the South American subhuman primates where you really do get malignant lymphoma.

DB That what I meant, in them.

AE Oh in them! Oh yes, but not in your African monkeys. We didn't know at the time that they were immune because of carrying something closely related.

DB You had a monkey colony of South American monkeys didn't you?

AE There are still in Bristol, yes, a very large percentage of the world population of this endangered species.

DB Now, when you got interested in looking for viruses you were only one of a lot of people. People sort of zoomed in from around the world because they all saw an opportunity of being the first person who could show that viruses could cause cancer in humans. And so there was intense competition, and nobody else, I think, had your idea of culturing tissue before looking at it. I think you were the first person who did that, weren't you?

AE Well, actually, there were really two things that I think led to our discovery. I mean, as I remember it there were really only three groups involved at the time. There was the group that came out and set up a lab in East Africa funded by the Imperial Cancer Research Fund, and there were the people in Western Australia, Stanley - Neville Stanley's people, but that was later. They were in Perth. And I think there was also [Gilbert] Dalldorf. He came out didn't he?

DB He did.

AE But none of them really got anything of any significance at all.

DB I don't know whether Dalldorf... You see Dalldorf's name was known because he had originally discovered the Coxsachie virus, I think.

AE He came out to Nairobi.

DB What he did I don't know quite...

AE Well, they were all interested in looking, and they all did things, but I think it's all forgotten because none of it was positive.

DB I suppose it's a little bit like, I sometimes think, trying to find your way out of a maze. If people go down false tracks and find that they are false tracks, they do make some contribution because nobody else need go down that track.

AE Absolutely. Everybody is putting a brick on the wall however small. It is the accumulation of bricks which makes the building.

DB I'm sure people who listen to this will want to know the event, the exciting event, how you suddenly discovered a virus and recognised it was a new virus and so on, because that must have been a very exciting occasion.

AE Well, it was really a combination of two things. I mean the first thing was that we spent months and months and months trying to isolate viruses from the material that you sent us, using all the standard techniques for virus isolation which were available in the early 1960s, which was when we were doing it. So that is putting them into hopefully sensitive tissue cultures, where one hoped that the virus would replicate; onto the chorionic membrane of embryonated eggs, where one hoped the same thing would happen as does and did with many types of virus; putting them into the brains of new-born mice and all this kind of thing. And none of it led to anything. And at the same time we were doing something which was extremely unusual at that time, we were looking at the material directly in the electron microscope. Now, of course that doesn't sound unusual at all today, but the number of people in the world doing electron microscopy then was very, very small. It was a small Mafia world-wide who all knew each other. And looking at the tumours directly we didn't find virus either. So we really had come to a dead end, as you say. And that made me think of one of the chicken tumours, and here we go back again to the viruses in chickens which cause cancer. And that was the erythroblastosis virus, where if you look at the virus infected cells directly from the body of the chicken you don't see

anything because the virus is there in latent form. But if you put those cells into tissue culture, even short term tissue culture, away from host defences, the latent virus switches on a virus replicative cycle and virus particles - what we now call virions these days - are made and you can find them in those tissue cultures. So obviously the thought was, well, if we can grow Burkitt's lymphoma cells in tissue culture maybe the same thing would happen. But that again was an absurd thing to try and do, because as you perfectly well know at that time no single member of the human lymphocytic family of cells had ever been grown in tissue culture. Well, we tried all the standard tissue culture methods and they didn't work. And I then remembered that some, I don't know, half a dozen years before, I had visited a man called Fisher at Yale University School of Medicine, who was working on mouse lymphoma cells. And he had shown me that if he took the cells directly from solid mouse lymphomas and put them into culture they wouldn't grow. But if he grew the lymphomas in the peritoneal cavity where they don't grow as solid lymphomas but as cells, single cells floating in the fluid which accumulates there in the peritoneal cavity of the mouse, and if you took those cells, the single cell suspension, and put them into culture he could grow them. So that's what gave me the idea that if we could set cells up as a single cell suspension they might grow in culture.

DB But this was a suspension of cells?

AE A suspension. But that again coincided with - the thought and the suspension of cells - with one of these accidents which have recurred all the way along the line. And this was on a Friday, the 5<sup>th</sup> of December - I am trying to remember what the year was - 1963, when the material you had sent us from Kampala did not arrive at Heathrow because there was fog and it was diverted to Manchester, so we didn't get it first thing in the morning because you used to send it overnight, on the Comet it was then; it was the Comet. And because of being diverted to Manchester it didn't get down to London until late in the afternoon, and it was a Friday afternoon and we got this specimen and it was about teatime. And I remember distinctly that it was about teatime, and I remember distinctly that it came in those little bijou bottles, 2 ml little bottles, in a suspension - in a sort of transit fluid is what I'm trying to say. And when we looked at this bottle, and of course nothing was frozen we didn't send anything frozen, and that's important because of course if it had of been frozen the cells wouldn't have been viable. So it hadn't been frozen, and we looked at this bottle and it was cloudy, very turbulent, opaque. And the thought naturally was, OK, this is an infected specimen and, you know, it's been travelling from Kampala for twenty four hours, it's sat about in the heat in Kampala before it got into the aeroplane - no freezing, you see. And since many of the tumours you were sending were from the nose and mouth obviously those were infected tumours, and the thought was: this is an infected specimen, it's not worth bothering with. And I remember somebody in the laboratory, who shall be nameless, saying, 'Oh come on, its four o'clock, it's an infected culture, Friday afternoon, chuck it away.' And I didn't actually, I simply took a pipette full, a micro-pipette full, and put it onto a slide, and slapped a coverslip on without any preparation and just looked down the microscope. And to my amazement there were no bacteria there. The turbulence was due to the fact that it was a very friable soft tumour and it had been shaken about on the journey and what was making the turbulence was a single cell suspension, cells that had been shaken free. And it was that made me think of Fisher and his mouse lymphomas grown as single cell

suspensions in the peritoneal cavity. And it was at that point that we put it up as a suspension culture, not in all the standard culture ways that we'd been doing without success before. And that's where the growing took....that was how it grew. That was the first one that grew on that Friday afternoon.

DB How easily it might have been lost.

AE Oh easily, yes. Chucked in the ....what we then used to use a Lysol bucket. Very old fashioned now.

DB You looked at it a few days later did you?

AE Oh no, we just left it. It took quite a long time to grow, it took several weeks. I mean, yes. I mean one of my very pessimistic collaborators was always saying, 'Oh this is rubbish, throw it away.' But at least it didn't have bacteria, it wasn't growing bacteria. And then suddenly we looked one day and the pH had changed and of course it was growing, and from that moment it took off.

DB And when did you find viruses in it?

AE That must have been the end of January that we had enough to look at.

DB Oh, it took you several...

AE Well, we were testing the cultures that we were growing by standard virological techniques, without any success whatsoever. And of course this is the second good thing, I think, of these sort of accidents, that was ours was one of the few laboratories in the world which used electron microscopy in parallel with biological testing. Because I had been - again another sort of accident though it was by design, actually - I had been to spend time with George Palade at the Rockefeller Institute in New York - it's now the Rockefeller University, of course - in order to learn electron microscopy at a time when it was hardly an infant; it was a new born, it was a neonate really. So having failed to isolate virus biologically, when we got enough cells to spare from these previous cultures, which we were terrified all the time of losing, we sacrificed enough cells to make an electron microscope preparation. And that's where the first grid square that I looked at, actually, had virus in it. It was obvious to me what it was. And again that was highly unorthodox because you couldn't possibly identify a virus by electron microscopy according to the dogma of the time, which was rubbish because for decades people had been identifying bacteria, looking down the light microscope. You couldn't say what kind of bacterium it was but you could say what family it belonged to. And in just the same way I knew damn well when you looked down the microscope, the electron microscope, you can perfectly well identify what family your looking at, and I knew at once that this was a member of the herpes family of viruses. Well, knowing that it was a herpes virus and a human herpes virus because it came out of your human biopsy material, I said to myself, this is not behaving biologically like a human herpes virus because any of the known herpes viruses of man at that time infecting cells would have replicated and wiped the culture out. That is exactly how virus diagnosis is made by a cytopathic, cytotoxic effect, and that had not happened. In fact, the cultures were growing while carrying this virus, so

immediately one knew that biologically this was something quite strange and different. I dare to say that I knew we had found what we were looking for. I mean one hadn't proven it but it was obvious.

DB What a fascinating story.

AE It was a series of accidents really. Lucky quirks.

DB Yes, so often that does happen.

AE That's right.

DB But you have to have two things: you have to have the accident as it were and the mind that can interpret them and look beyond them and see their meaning.

AE Well, of course that's what Louis Pasteur said wasn't it: 'Chance favours the prepared mind' - inscribed on the dome of the Harvard Medical School.

DB Fortunately, there was a prepared mind there. Well, what did you do with your cultures then, the next stage along the line?

AE Well, we grew them up and of course were working with them. I remember we did all sorts of weird things. We were talking earlier about the idea that it might be that this virus was dependent for its temperature and rainfall distribution, as we thought, not correct, but we thought because it was spread by an arthropod vector. Well, I can remember doing endless experiments in which we had mosquitoes and we were trying to coax them not to feed on blood, but to feed on our virus carrying cultures in the hope that they would in turn become infected and there would be a replicating phase in the mosquito, as with all arthropod borne viruses. And we had an awful lot of fun, I remember, because you had to provide them with an appropriate membrane to pierce with the food behind. And it had to be warm or they wouldn't go near it, so we had a heating device. We tried gold beating - gold beater's membranes, something made out of guts; we tried French letters; we tried everything, and we got them to eat the stuff but of course the virus didn't replicate because that was another dead end. All these experiments were going on.

DB But it's terribly important to show that it didn't grow. If you had been able to show that it did grow in insects, that would have put us on the wrong track altogether.

AE Exactly. Well, it didn't. But all this time we were doing all the necessary things to try and identify human herpes virus; again in tissue culture, in mouse brain, on embryonated eggs and it wouldn't grow in anything. And I remember, we discussed this in the lab: perhaps we're doing some stupid little thing which is inactivating it each time, perhaps we are just making some error; we must get this corroborated that it won't grow in these standard ways. And I went to two British groups who were experts in herpes virology and neither of them wanted to know: this was all a load of rubbish; you can't identify viruses with the electron microscope; you haven't got a herpes virus there, if you had a herpes virus it would grow. And that was the sort of climate that one was operating in, and it went on for some years. So,

having tried in the UK which I badly wanted to have British people involved, we sent it to scientific friends, the Henles in Philadelphia, who were avid to have it and to look at it. And they also were unable to show that it was an ordinary human herpes virus with all the standard tests and indeed we published a joint paper in, I think, the *Journal of Experimental Medicine* after that which really did show that this was something quite unusual and new. And, I mean, that established it biologically which was the best you could do in those days. Of course, now we know at the molecular level and all the rest of it. Immunologically next, that we did next, yes. The Henles did it and we did it also.

DB It's a little aside if I could bring in there: in 1962 Evelyn Coop - we used to call him Chick Coop - came to our home in Kampala and I showed him some of the patients we had. And he was of course the senior surgeon at the same hospital as the Henles worked in.

AE That is right. He became Surgeon General in the United States, yes.

DB But he went back to Philadelphia and said to the Henles, 'I've a hunch that if you want to look at a tumour that might contain viruses, this might be the one.'

AE Well, that's good because it was just about that time that we sent the material to them and they were very receptive.

DB And then of course coming out of that there was the quite remarkable serendipitous story again: how they discovered that your virus was the cause of infectious mononucleosis.

AE Oh, that's right.

DB Well, tell us that story.

AE Well, that's quite an amusing story, another of these little accidents, you see, that have - dogged isn't the right word - helped promote this story all the way. Yes, that's right. Now, what was that? There was a man called John Paul, who was professor at Yale University School of Medicine, who had been working on infectious mononucleosis, glandular fever, for perhaps two decades. I think he started before World War II and they really had got absolutely nowhere with it. Nobody could understand this curious disease. But what they did have was a large collection of serum samples from patients, and from people before they became ill, and from people when they became ill, and afterwards and so on, and all that was away in the deep-freeze, because they had been studying cohort intakes of new students at Yale. So they had all this material and they really didn't know very much what to do with it. And while the Henles were working on the virus that I'd sent them, which they actually called EB virus, they named it Epstein-Barr virus, after Yvonne Barr of course who was a PhD student collaborating in our lab at that time. Well, while they were working on it, one of their technicians Elaine Hurtkins got infectious mononucleosis. And they were trying to set up an immunofluorescence test for antibodies and, of course, for that you always have to have a negative control. And they'd been using Elaine Hurtkin's serum, serum yes, as a negative control. She didn't



have a bad attack. She was away about two weeks and she came back again and she resumed her work.

DB This wasn't in the Henles' laboratory was it?

AE No, no, this was in the Henles' [laboratory]. Elaine Hurtkins was one of the Henles' technicians, a very pretty girl, which of course is also part of the story. And she came back after two weeks and resumed the immunofluorescence studies, and again had a tiny serum sample from her own blood as a negative control, and it was no longer negative. So the penny dropped, and they said 'Good heavens, something has happened to her in relation to this recent attack of infectious mono[nucleosis].' So then they thought of Jean Paul and they drove straight up to Yale. And they got all these serum samples out of the freezer and were able to show that people before they had their attack of infectious mononucleosis had no antibodies to EB virus, and during and after the attack they developed antibodies and maintained them. So, I mean, that put the connection that infection with EB virus was associated with infectious mononucleosis. I mean the point about her being a very pretty girl is that it had been known as the 'kissing disease' for a very long time and nobody, of course, knew why, but it was associated with deep kissing amongst young adults and adolescents. And she was a very pretty girl and she picked the virus up in that way, not from a laboratory infection, of course. So she was really like that little boy of Jenner's that he did the first vaccinia experiment on. What was his name? James....it's gone.

DB I know the story but I can't remember the name.

AE What is his name? It will come to me in a minute. So she's gone into the literature in that kind of way.

DB Now having gone through that frightfully...

AE Phipps. James Phipps.

DB ...that frightfully interesting story, let's turn back a moment to when you came out to make further discoveries in Africa. Now, do you remember the occasion when we set out over Lake Victoria together?

AE We went to the Sese Islands.

DB The Sese Islands. And we sort of bribed local inhabitants. We said we'd give them so many shillings if they could collect a monkey, a live monkey, and they collected live monkeys for you.

AE That's right.

DB And then, if I remember rightly, I think we went to more than one island, but it was dark when we set out to go home. We went over on a motorboat, I mean a sort of regular thing.

AE Oh sure.

DB But the only way of getting back was by canoe.

AE We were in a dugout canoe.

DB And we got in a dugout canoe, which had a rather faulty engine, outboard motor at the back. It was pitch dark, we had about eight miles to cross over the lake, the motor almost gave out.

AE It did give out. No, it gave out! We were drifting.

DB And we got it started. They got it started again.

AE It took a long time. We were in the middle of that lake.

DB Crocodile infested lake.

AE And famous for its sudden storms.

DB Yes, that is right.

AE But it was, I remember that it was a marvellous velvet black sky with an extraordinary display of stars, and very slowly we watched a Sputnik go over. That was the first man-made satellite I'd ever seen. It was a Russian Sputnik that went over. It was extraordinary, absolutely extraordinary.

DB The remarkable thing was too, of course, the canoe chap had nothing in the way of a compass or anything and yet in the black darkness he arrived exactly where he wanted to land on the shore the other side.

AE There wasn't a landing station Denis. We had to go through it. I've never been so eaten by mosquitoes in all my life. Actually, that was amazing. No we were drifting for hours.

DB Yes we were.

AE Yes, we didn't get back until the small hours of the morning.

DB Late at night. But again, you see, that was an example of the last sort of experience that people associate with medical research. Medical research is associated with white coats, albino mice and laboratories and so on.

AE And syringes.

DB But these are the instances that bring it to life and make it such fun. So what did you do with these monkeys when you've got them?

AE Well, these were the monkeys that we put the tumour material into in the hope of transmitting the virus, but of course they were the African green monkey,

*Cercopithecus aethiops*, which has its own EB like herpes virus, a very closely related cousin. And the genetic overlap is sufficiently close for the antibodies against the monkey virus to be cross-reacting with the antibodies against the human virus, and they were therefore already infected and it was a hopeless experiment. But nobody knew that.

DB Several of them got lumps later on but they didn't turn out to be tumours.

AE They didn't really turn out to be the right thing.

DB Great excitement at the time.

AE They didn't turn out to be the right thing.

DB Now, what have been the major - you see, this is as far as my understanding and knowledge went - what have been the major events that had happened since 1964? In 1964 you published your first paper<sup>1</sup> and poor old Bert Achong got left out of the name which is something of a pity.

AE Well, he did but he's the second author on the paper and wherever I've got any kind of historical survey I always have his picture and Yvonne Barr's picture.

DB Because he worked with you for about twenty years.

AE That's right. Yes.

DB Now, that is nearly thirty years ago. Now, in a nutshell, I don't know how long you want to talk about what's happened since then.

AE Well, I mean, what's happened since then: God, there's just been an explosion. It's become a subject, EB virology is a subject on its own. There are international meetings devoted to EB virus and its an explosion. I mean, you've only got to look at the cumulative index or something for a month, let alone a year, to see an absolutely enormous amount of work. I mean, I suppose the main things are really the understanding of the molecular biology, which is now allowing people to dissect the genes and look at the gene products and see what these gene products are actually doing in functional terms, which is giving very good insight into how the virus transforms normal cells into continuously growing immortalised cells, and which is beginning to show... Well, there are two possible scenarios as to how it induces tumours *in vivo*. So I mean that is coming along extremely fast, extremely fast.

DB So, the important thing is work is most valuable if it turns out to be a sort of catalyst which initiates all sorts of other work in associated fields. You see this work and your virus has gone far beyond a particular tumour. It's had implications on viral oncology in general in a much wider field, hasn't it?

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<sup>1</sup> Epstein, M A, Achong, B G, Barr, Y M. 1964 *Virus particles in cultured lymphoblasts from Burkitt's lymphoma*. Lancet i p.702-703.

AE I think that's absolutely right. And of course it isn't now a particular tumour. I mean, it's not just Burkitt's lymphoma; it's undifferentiated nasopharyngeal carcinoma, which I hesitate to say this, but in world cancer terms is more important than Burkitt's lymphoma.

DB Oh, far, far more important.

AE In terms of numbers, but not in terms of being the 'Rosetta stone' for the whole subject as Burkitt's lymphoma was.

DB I can remember you mentioning - I think it was when we were together in Trinidad - that nasopharyngeal cancer was the commonest cancer of men and the second commonest cancer of women in the most populated part of the world, in South East Asia.

AE That's absolutely correct.

DB And in that context it becomes enormously...

AE But, I mean, in terms of theoretical considerations, Burkitt's lymphoma is the 'Rosetta stone'. In terms of world tumour numbers the virus does have a role.

DB How are things getting along with the possibility of a vaccine?

AE Yes, well how? As you know that has been my preoccupation for the last dozen years. And we do have a vaccine antigen, a molecule, purified molecule, which will powerfully protect the South American monkeys that we were talking about as being susceptible to the virus, powerfully protect them from a 100% tumour inducing challenge dose of virus. So that is there. There are administrative difficulties in getting moving, and financial, towards a human trial. But I am rather pleased that there is to be a large meeting in - not large numerically of participants, rather than of possible funding agencies. There are going to be about twenty five possible funding agencies in the United States in New York next month to try and get together a practical plan for a human vaccine trial. I mean, that I think looks very hopeful indeed.

DB This I think is enormously important because I feel increasingly in my own field and studies, that the only hope of reducing the incidence rates of any form of cancer is going to be along the line of prevention.

AE Oh, sure. Oh, yes

DB And you see at the moment nearly all the money goes into diagnosis and cure, and by the very nature of things no form of cancer ever will be reduced in frequency by improved diagnosis and by improved treatment; it's got to be prevention. Now, they have started off haven't they - I know that you know all about this - they're started of trials in hepatitis B vaccine for liver cancer?

AE Oh, that's right. Oh, sure.

DB Now if your virus, your vaccine could eventually be protective against nasopharyngeal cancer, and if hepatitis B virus could be protective against liver cancer, there you'd have enormous advances in cancer. Whereas, from the point of view of therapy, other than children's cancer, the advance, progress has been very undramatic.

AE Well, I don't know. Well, I mean I can think of several cancers which were a death sentence when I was a student where there is a 90% survival rate now.

DB But not in the common cancers.

AE No. No, that's true.

DB You see, when one comes into the terms of prevention, you see, if you take - we're going a little bit of balance but it is appropriate - the common cancers in the western world, which are rare in the Third World, are: lung, prostate, bowel and perhaps ovary. And a recent study, which is I think coming out in the National Cancer Institute very soon, they have done a twenty five year study with enormous numbers of Seven Day Adventists, who are non-smoking, vegetarian [having a] high fibre diet, and those are the very cancers which they have lower rates of.

AE Yes. Well, it is not straying from the virus. I think that the point you are making about cigarettes is exactly analogous to the virus situation. I mean, the vaccines you've mentioned, the hepatitis B and hopefully our vaccine do not act against, are not intended to, or thought to act against the tumours. They're not anti-cancer, they're preventive. They are to prevent the infection with the virus which is the putative cause. And it is the same as the cigarette; you remove the cigarette from the equation, the putative cause, and the lung cancer decreases.

DB You talk about difficulty in getting funding; it's far easier to get funding for therapy than funding for prevention because somebody is going to make some money out of it.

AE Well, I mean on the other hand the hepatitis B vaccine virus trial is going forward.

DB So I gather.

AE Of course, it was very easy - well no, I take that back - it was relatively easy to have a hepatitis B vaccine because there's tons and tons of surface antigen in the peripheral blood of infected persons, and all you've got to do is purify it. But I mean to purify the molecules that could be used in EB virus vaccine was really quite a sweat, that was a long hard haul. But no, I think the cigarette smoking one is an exact parallel. We do not know exactly how cigarette smoke causes cancer, but we do know that if you remove the cigarette from a very complicated chain - not just a direct effect, a chain of events - if you remove that one single link in the chain, the incidence of lung cancer decreases. And I believe that exactly the same thing will be shown if you remove hepatitis B virus for another very complicated chain of events.

DB EB virus?

AE Or EB virus. And the chain is not understood but the evidence is; the virus is necessary, although not on its own sufficient. But without it you don't have the continuous chain. And if you can remove that by vaccinating to prevent infection, I think it's exactly parallel to the cigarette and bronchogenic carcinoma story. Exactly.

DB The important thing in the whole of this, to me, that is once you can identify a important factor in cancer you don't have to understand mechanisms in order to get results. If you can identify causes and remove the causes, you don't have to understand mechanisms. I've often thought of the story with scurvy, where you see James Lind first of all showed that scurvy could be prevented by giving people fresh fruit and vegetables. It wasn't till nearly half a century later that it was tried out on the British Navy by Gilbert Blane...in large numbers. And they found out that by giving ships going to sea, I think it was sauerkraut, they reduced more casualties than had previously been attributable to all other diseases, all battle casualties, all shipwrecks and almost doubled the fighting force of the British Navy. Not until one hundred and fifty years later, 1932 I think, did they understand that it was ascorbic acid.

AE No I absolutely agree with this, and I have to say that a great deal of criticism of the idea of a vaccine, I mean of an EB virus vaccine, was based on the fact 'Oh, but you don't know how it works'.

DB Absolutely.

AE But then if you waited to find out how cigarettes cause lung cancer before telling people to stop smoking it would be a disaster. But the other thing, you see, about a vaccine trial is that if you have a putative virus cause for a human cancer, the only way that you can actually prove that that is the cause, the only way is - because as many monkeys as you like to work with are not the same as humans - the only way is to vaccinate, remove the virus and show that there is a decrease in the tumours in a vaccinated population. And I mean, you know, the two things are not only...I mean if you must insist on that experiment, well a vaccine trial will do it for you.

DB Well, it will be awfully exciting to see this coming along. But as you look back, Tony, on your life, if you had been worried by or listened to your critics you would have been put off.

AE Oh, no, no. Never pay any attention to that. I mean they don't understand, Denis.

DB Because you're unlikely to make any worthwhile contribution unless somebody tells you you're a bit of a fool and a nitwit, aren't you?

AE Yes. Well, we did a lot of very stupid things along the way.

DB You only make progress by acknowledging mistakes.